Chapter 104

Nutrition and Amyotrophic Lateral Sclerosis

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LIST OF ABBREVIATIONS

AC  arm circumference
ALS  amyotrophic lateral sclerosis
AMA  arm muscle area
AMC  arm muscle circumference
BIA  bioelectrical bioimpedance analysis
BMI  body mass index
DXA  dual-energy X-ray absorptiometry
FA  fat area
FTD  frontotemporal dementia
MND  motor neuron disease
PA  phase angle
PE max  maximum expiratory pressure
PEG  percutaneous endoscopic gastrostomy
PI max  maximum inspiratory pressure
TS  triceps skinfold

INTRODUCTION

Changes in nutritional status can accelerate the disease progression and alter the survival time of patients diagnosed with amyotrophic lateral sclerosis (ALS). We will describe the nutritional treatment, including assessment of the nutritional status, dietary characteristics, and indications for nutritional supplements and enteral therapy. Additionally, some clinical factors must be considered for the nutritional therapy in ALS.

AMYOTROPHIC LATERAL SCLEROSIS

ALS progresses to general motor impairment. The main physical change is muscle loss in the limbs, abdomen, and oropharyngeal and laryngeal regions, which is associated with the effects of muscle degeneration [1,2]. In advanced stages, there is decreased respiratory muscle strength, dysphagia, and weight loss [3].

The mean survival from the onset of symptoms is 3–5 years [4]. Currently, there is no cure for the disease. Several treatments have been tested, with no significant changes in the natural history of ALS [5]. Clinical trials seek to find treatments that produce a positive impact on ALS by increasing the life expectancy and slowing the disease progression.

From a nutritional perspective, the body weight loss associated with bulbar changes (dysphagia and respiratory difficulty) demonstrates the need for early nutritional care [5].

The decreased food intake is caused by several factors, such as a lack of appetite, dysphagia, weakness, dyspnea, and depression.

Dysphagia, which is characterized by difficulty in the passage of a swallowed bolus from the mouth to the stomach, may manifest itself differently and in different moments within the clinical course of the disease and varies according to
the consistency of the food. Patients with motor neuron disease (MND) initially present with difficulty with thin liquid food consistency, which may compromise their hydration. The weakness of the masticatory muscles may cause patients to have difficulty with hard solids, such as meats. The weakness of the lips, tongue, and buccinators may hinder the oral bolus propulsion, causing difficulties with thin liquids, dry solids, and food with dual consistencies.

Changes in the consistency and viscosity of the diet sometimes lead to the exclusion of high energy and protein foods, especially in ALS patients with a predominant bulbar involvement [6].

Muscle atrophy may mask the increased metabolic demand, which is characteristic of progressive diseases. The increased basal energy consumption in patients with ALS occurs because the energy is used to maintain pulmonary ventilation [2–4].

Similarly, studies have shown increased energy expenditure at rest in 10% of these patients when compared to the healthy population, which is characteristic of an increased metabolism. In more advanced or terminal stages, these values are even higher [7–9].

The causes of hypermetabolism in ALS are not well understood. To date, the accepted causes are related to the reduction in lean body mass. The initial hypothesis to explain this paradox would be the increased respiratory muscle activity to maintain adequate gas exchange [1,7,10]. A possible mitochondrial involvement in the hypermetabolism in ALS has been the focus of recent studies [2,8,9].

Based on analyses of changes in body composition, the increased body weight can compensate for the energy consumed in the reduction of lean body mass during the disease progression [3].

The body weight reduction is frequent, and dietary factors are involved. One study observed a loss of 2 kg of lean body mass within 6 months in patients with an adequate food intake according to their needs. Another study found that weight loss did not occur in all patients, suggesting that the reduction of food intake could not be simply attributed to inadequate food intake or muscle atrophy [1,11,12].

In the 1980s and 1990s, a weight reduction of 10% or more within 3–6 months would be considered the trigger of physiological changes and morbidity [1,7]. The weight loss during the survival time of patients with ALS became so severe that studies tried to identify it as a predictive factor. A recent study reported that a 5% decrease in normal weight on diagnosis increased the risk of death by 30% [13].

The reduced food intake, increased energy consumption, and loss of body fat reinforced the importance of nutritional intervention in ALS patients [2,5,7,9,11,13–18].

**NUTRITION AND ETIOLOGY OF DISEASE**

To date, information on the role of food in the etiology of ALS or as a protective or progressive factor for the disease is limited. When analyzing the ingestion of calories, proteins, lipids, and carbohydrates with a focus on some amino acids, micronutrients (vitamins A, C, and E, zinc and copper), and fiber, the results showed a significant difference only for the ingestion of lipids and soluble fiber [19].

For the ingestion of lipids, similar data were found for another neurodegenerative disease: Parkinson’s disease [20]. Regarding the ingestion of soluble fiber, the relationships remain unknown.

Regarding carbohydrate metabolism, some authors suggest glucose intolerance and reduced insulin levels. The alteration in the glucose levels is inversely proportional to the severity of the disease, suggesting that the insulin antagonism is not the first abnormality of ALS but that it could be related to the physical inactivity present in progressive diseases [21,22].

It is not uncommon to observe an abrupt elevation of serum lipid values. Gustafson and Stortebeker found hypercholesterolemia in some patients in the initial stages of the disease and hypertriglyceridemia in several terminal patients [23].

Reinforcing previous findings regarding lipid metabolism in MND/ALS, Dupuis et al. [22] and Dorst et al. [24] found that the increases in cholesterol and triglyceride levels have a protective role in the progression of the disease in animal models. Therefore, treatments suggested for controlling dyslipidemia must be reconsidered in patients with MND/ALS.

Regarding protein metabolism, some studies have found changes in the absorption and serum levels of arginine, while others have suggested increased serum levels of other amino acids, such as tyrosine, lysine, and leucine in MND/ALS [1,18].

Studies with strong evidence of ergogenic applications for the use of carnitine and creatine in humans were not found [18]. The use of branched chain amino acids (L-leucine, L-valine, and L-isoleucine) and L-threonine is contraindicated in the treatment of MND/ALS. The branched chain amino acids are glutamate antagonists and would theoretically act against neurotoxicity. A study investigating the effect of branched chain amino acids was interrupted due to the mortality and decline in the forced vital capacity (FVC) [25].

Low levels of vitamin D are also observed in patients with MND/ALS. The inability to sunbathe at home and the lack of weight-bearing physical activities for prolonged periods in bedridden or hospitalized patients, combined with reduced food
intake, determine this condition, which increases the risk for osteoporosis [26]. Some other biochemical changes, which are observed in other neuromuscular diseases, also occur, resulting in muscular destruction. Among them, changes in the serum levels of sulfur, potassium, magnesium, and zinc are observed [27].

Some patients seek alternative treatments and self-medicate, using vitamins, herbs, and dietary supplements. Studies on the use of nutraceuticals and functional food to prevent and treat MND/ALS and other degenerative diseases are the focus of some researchers [25]. Most of these studies are experimental, with no pre-established doses and few conclusive results. This factor limits the safe indication of these substances for the treatment of ALS.

NUTRITIONAL EVALUATION

The nutritional evaluation includes the clinical history, eating habits, anthropometric measures, and biochemistry data. The measures used are weight, height, circumferences, and skinfolds (Table 104.1). The body mass index (BMI) is calculated using the following formula: weight (kg)/height (m^2). Values between 18.99 and 24.99 kg/m^2 [27] are considered normal and are associated with a lower morbidity-mortality rate. Because the values for BMI increase with age, specific guidelines have been suggested to calculate the BMI of elderly patients [28].

The anthropometric measures and indexes commonly used for nutritional assessment in MND/ALS are body weight, weight loss percentage, and BMI; these measures do not reflect specific changes in the body compartments [16].

To collect more precise information on the body composition, additional data must be considered, such as the skinfold and circumference measures. Biochemistry data are also included in the nutritional assessment. When compared with the clinical signs, the nutritional status may vary slowly, showing that the biochemistry analysis is valid but that its results must be carefully interpreted. The biochemistry data that are commonly used to evaluate the nutritional status are serum levels of albumin, transferrin, and retinol-binding protein.

Anthropometry, bioelectrical impedance analysis (BIA), dual X-ray absorptiometry (DXA), and doubly labeled water are the most common methods used for nutritional assessments in studies. Except for anthropometry, these methods are mainly used for clinical trials [14,16].

A pioneering study on the nutritional assessment of ALS patients described a decreased arm circumference (AC), arm muscle circumference (AMC), and triceps skinfold [1]. In a study on the assessment of the nutritional status by different methods, the bioelectrical impedance and the anthropometry did not show significant differences [29].

An analysis of the phase angle (PA) by the BIA has been described as a prognostic factor for the survival time of patients with ALS. The PA was significantly lower in malnourished ALS patients than in non-malnourished patients. The patients with a PA < 2.5 had a poorer survival rate than the patients with a PA > 2.5 [30].

No differences were found in the measures of water percentage, fat percentage, and lean/fat ratio measured by BIA. However, in the group of patients with bulbar compromise, we observed a slight increase in the percentage of body water, indicating that part of the weight gain is due to the increase in the body water during the process of nutritional maintenance or repletion [29] (Figure 104.1).

Regarding the body fat, in the absence of any adverse metabolic status, the ability of the adipose tissue to recover after a mild malnutrition situation exceeds the values found in adequate nutrition. Fat replenishment is also more easily achieved by the body than the rebuilding of the lean body mass under adequate nutrition. The maintenance of body fat in ALS can compensate for the loss of energy that was consumed by the muscle tissue [11].

<table>
<thead>
<tr>
<th>TABLE 104.1 Anthropometric Measures Used to Evaluate the Nutritional Status of the ALS Patients</th>
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<tbody>
<tr>
<td>- Weight</td>
</tr>
<tr>
<td>- Height</td>
</tr>
<tr>
<td>- Arm circumference (AC)</td>
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<tr>
<td>- Arm muscle circumference (AMC)</td>
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<tr>
<td>- Arm muscle area (AMA)</td>
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<tr>
<td>- Fat area (FA)</td>
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<tr>
<td>- Triceps skinfold (TS)</td>
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Although previous studies suggested specific methods for nutritional assessment, most professionals use the BMI [31–34]. There are consistent reports correlating the BMI and the disease progression [10,13,14,31,32,35,36].

When analyzing the changes in the nutritional status as a prognostic factor in patients with MND/ALS, a reduction of 5% in body weight at the time of the diagnosis was associated with a 30% risk of death. If the weight reduction occurred during the follow-up, the risk increased to 37%. For the BMI, a reduction of 1 kg/m² was associated with a 20% risk of death [13].

The changes in the nutritional status during the disease progression are well known. Studies have demonstrated decreased body weight, fat and lean mass, in addition to the increased energy expenditure at rest, even with an adequate ingestion of protein and energy [6,8,11,13,29,34,36]. One of the factors that contributes to the increased energetic expenditure is an increased respiratory rate, which is a compensatory measure to maintain the tidal volume.

**NUTRITIONAL SUPPORT**

**Oral Proceedings**

With or without cognitive changes, patients with alterations in the oral or pharyngeal phase of swallowing can have difficulty eating. A history of cough or hoarseness during or after meals, the presence of wet voice after swallowing, the referred feeling of food stuck in the throat (larynx stasis), nasal reflux, anterior and premature food spillage, residual excess in the oral cavity after swallowing, and an increased time of intake are associated with weakness of the oropharyngeal and laryngeal muscles. The observation of some signs and symptoms during meals allows a nurse or nutritionist to perform an initial tracking as triage for detecting a risk of dysphagia and bring the signs to the attention of the health team.

The dysphagia or difficulty to swallow is a common problem in patients with MND. In addition to the oropharyngeal and laryngeal weakness that determines changes in the biomechanics of swallowing, there are associated factors that may trigger or even aggravate the dysphagia condition, such as increased volume and viscosity of the saliva, decreased peak values of the cough flow, hypo- or hyperreflexia, loss of inspiratory and expiratory muscle strength (PImax and PEmax, respectively), and occurrence of respiratory or muscular fatigue. As a result, the patient may have repeated respiratory infections, weight loss, and anorexia.

Because it requires maximum coordination and control, the greatest difficulty in swallowing is associated with fluid intake. An inability related to lip pressure and tongue control, premature spillage, a reduction in the laryngeal elevation, and pharyngeal muscle weakness may underlie difficulty in the coordination between the oral and pharyngeal phases of swallowing, leading to laryngeal penetration or aspiration. Therefore, thin liquids should be avoided. To meet the water requirements, thickening liquids with natural thickeners, such as mucilage, or commercial thickeners, such as Thickeasy® or Thick-up®, is recommended. An alternative would be to offer fluids as fruit juices with two fruits, such as papaya with orange or papaya with acerola, or thicker juices, such as watermelon, mango, and peach. Initially, transitioning from a thin liquid to a nectar consistency is sufficient to minimize the occurrence of gagging with liquids [36].
The consistency of food should be modified according to the difficulty of swallowing. Commonly used adaptations are thickening the thin fluid, cutting the food into smaller pieces, preferentially consuming soft and wet food, switching between liquids during feeding (to facilitate cleaning of the pharyngeal recesses), and mixing two consistencies as a facilitating measure. As the difficulty in chewing and swallowing increases, the liquid must become thicker, and the solids should be doughy and homogeneous. Throughout the course of the disease, the amount of food ingested orally decreases due to fatigue. Table 104.2 shows the main characteristics of the prescribed diet.

From diagnosis, the patient is enrolled in an energy-conservation program in which the energy expenditure should be monitored based on the activities performed, alternating activity and rest so that fatigue is not deleterious, which would soon deprive them of autonomy in their daily activities.

The nutrient supply must be guaranteed at all times, and the nutritionist should prescribe supplements to complete the caloric value of the diet when necessary. The evaluation and the therapeutic speech and language therapy monitoring are measures recommended to ensure that the food is safe and effective for the patient.

An early adoption of the nutritional therapy can prevent the depletion of body resources, especially body fat, and thus mitigate the loss of lean body mass [6,7,16,30,32,37,38].

In the early stages of the disease, the use of nutritional supplements and the multidisciplinary approach, including dietary intervention, are the best measures to increase food intake. To achieve values between 100% and 130% of the nutritional recommendations, prescribing energy and protein supplements in addition to the usual diet is recommended [29] (Figure 104.2).

### ENTERAL NUTRITION

Enteral nutrition may be required to meet energy requirements or when oral feeding is not safe. In most cases, the gastrointestinal tract function remains intact, and enteral nutrition, instead of parenteral nutrition, is the method chosen for nutritional support.

Although the nasoenteric probe is an option in the short term, percutaneous endoscopic gastrostomy (PEG) is preferred for prolonged treatment.

For MND/ALS, PEG is the main method of accessing the digestive tract for the purpose of nutrition [5,7,15,39–41].

PEG is a choice for symptomatic treatment, providing adequate nutrition, weight loss stabilization, and an alternative for the administration of fluids and drugs, and allowing oral nutrition when possible [17,42].

Patients with MND/ALS benefit from the endoscopically inserted gastrostomy tube because the procedure does not require surgical intervention, general anesthesia, or invasive ventilation [43] (Table 104.3).

The criteria for indicating PEG in MND/ALS are reduction to approximately 50% of the predicted forced vital capacity, moderate dysphagia, and 10% reduction in body weight. The vital capacity measure would be the variable of choice for the success of the procedure. With less than 50% of the predicted values, there is a risk of hypoxia during the procedure [44–46] (Figure 104.3).

A limitation of PEG is observed in patients with moderate respiratory compromise or severe spasticity of the masseter [35,42]. Another method is the insertion of a gastric tube by radiology [8,47].

Although the criteria for PEG are clear, the ideal moment for placement remains unknown. The weight loss and worsening of dysphagia can be controlled by modifying the food consistency and prescribing nutritional supplements. The reduction in FVC appears to be the earliest criterion indicating PEG. Some studies also emphasize the early indication of PEG in patients with neurobehavioral dysfunction [48].

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**TABLE 104.2 Characteristics of the Diet Recommended to the ALS Patients**

<table>
<thead>
<tr>
<th>Requirement</th>
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<tr>
<td>Fractionated into 6 meals/day</td>
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<tr>
<td>Food with doughy or pasty consistency</td>
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<tr>
<td>Small amounts</td>
</tr>
<tr>
<td>Hypercaloric</td>
</tr>
<tr>
<td>Hyperproteic</td>
</tr>
<tr>
<td>Normolipidemic to hyperlipidemic</td>
</tr>
<tr>
<td>Rich in fiber</td>
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</tbody>
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New nutritional evaluation

Malnutrition  
Eutrophy  
Overweight/obesity

Oral nutritional supplementation  
Orientation

Reassess the nutritional status

Weight loss

Yes

>10%

No

<10%

Orientation

PEG  
Oral nutritional supplementation

FIGURE 104.2 This flow chart aims to optimize nutritional support for ALS patients [29].

TABLE 104.3 Criteria for Indication PEG in ALS Patients [44]

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Description</th>
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<tbody>
<tr>
<td>Nutritional</td>
<td>Loss weight ≥10% in three months</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>Worsening mild to moderate</td>
</tr>
<tr>
<td>Respiratory</td>
<td>FVC &lt;50%</td>
</tr>
</tbody>
</table>

FIGURE 104.3 Nutritional status of 33 Brazilian ALS patients, 2009.
APPLICATIONS TO OTHER AREAS OF COGNITIVE DECLINE

Traditionally, cognition has been considered to be preserved in patients with ALS. However, it is now recognized that 10–50% of patients with ALS present with a subtle cognitive decline and that 10–55% have an overt frontotemporal dementia (FTD). Compared to ALS with spared cognition, patients with ALS–FTD are reported to have reduced survival [49,50]. In those cases, PEG should be indicated earlier [48].

There is minor evidence of increased survival time after PEG because the manifestation of the disease may be a negative predictive factor. In ALS, the nutritional aspect is believed to be an independent prognostic factor that requires intervention from the moment of diagnosis, regardless of the symptoms or signs related to the disease progression.

Currently, there is no cure for ALS. Several treatments have already been tested, including antioxidants, calcium channel blockers, antiviral agents, inhibitors of excitotoxicity, plasmapheresis, and immunosuppressants, without any significant change in the natural progression of ALS. From the beginning, the nutritional orientation slows the loss of lean body mass, and it is currently the most consistent factor related to increased survival time [5].

PRACTICAL ISSUES

Nutritional support in ALS patients is part of medical treatment and should be started early. Assistance through dietary changes, such as fractionation of meals, calorie and protein food inclusion, prescription of supplements, can prevent changes in body composition, especially in body fat. The nutritional evaluation through anthropometric measurements, especially the arm measures, may reflect the body changes and allow those quickly.

Nutritional therapy with calorie and protein supplement should be initiated for patients who don’t get to keep the oral diet. When it is not possible to maintain the patient’s oral diet, then enteral nutritional therapy for these patients is indicated through PEG. For patients with cognitive decline, all guidelines should be carried out as early as possible, before the appearance of the symptoms or change of nutritional status.

SUMMARY POINTS

- ALS is a disease that leads to increased basal metabolism and is a result of nutritional needs. Low food intake may present changes of nutritional status.
- The diet prescription should be adequate during the course of the disease, according to individual needs and must also be accompanied by food intake and, when necessary, make dietary fixes.
- Maintain adequate ingestion of calories and protein to meet the nutritional needs of individuals.
- Maintain adequacy of protein and calorie intake, and when necessary, recommend the use of nutritional supplements. You must use reliable products designed for clinical conditions and not sport.
- Following the proposed criteria for enteral therapy in patients with ALS, make a statement early. The best solution is to indicate the PEG in place of the enteric tube.
- It is recommended to prevent weight loss or changes of body composition in ALS patients. The ideal is to promote body fat gain to reduce the loss of muscle mass.
- All efforts should be directed toward maintaining the nutritional state, contributing to medical treatment and survival of ALS patients.

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REFERENCES


